Weather and air pollution as triggers of severe headaches

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ABSTRACT

Background: The roles of weather conditions and air pollution as triggers of headache have been inconsistent in previous, generally small studies.

Methods: We performed a case-crossover study of 7,054 patients seen in a single emergency department between May 2000 and December 2007 with a primary discharge diagnosis of headache. We compared levels of temperature, barometric pressure, humidity, fine particulate matter, black carbon, and nitrogen and sulfur dioxides during the three 24-hour periods preceding presentation with corresponding levels on the remaining occurrences of that day of the week in a given month, using local meteorologic and pollutant monitors.

Results: Higher mean ambient temperature in the 24 hours preceding hospital presentation positively and linearly increased the acute risk of headache (odds ratio [OR] for a 5°C increment 1.075; 95% confidence interval [CI], 1.021–1.033; $p = 0.006$). Higher risk was observed for cases with and without a discharge diagnosis of migraine and for cases between October and March or between April and September. Lower barometric pressure also increased the risk of nonmigraine cases in the 48 to 72 hours before hospitalization (OR 0.939 per 5 mm Hg; 95% CI, 0.902–0.978; $p = 0.002$). Current levels of pollutants did not influence the risk of headache.

Conclusions: Higher ambient temperature and, to a lesser degree, lower barometric pressure led to a transient increase in risk of headache requiring emergency department evaluation. We did not find clear association of air pollutants with risk, but cannot exclude effects of air pollution of the magnitude previously observed for stroke and other cardiovascular events. ***Neurology*® 2009;72:922–927**

GLOSSARY

BC = black carbon; **BIDMC** = Beth Israel Deaconess Medical Center; **CI** = confidence interval; **OR** = odds ratio; **$PM_{2.5}$** = fine particulate matter with aerodynamic diameter ≤2.5 μm.

Migraine and other headache syndromes represent an enormous source of morbidity, especially among young and middle-aged adults.[1] Approximately 18% of women and 6% of men in the United States report migraines,[2] and annual costs attributable to migraines have been estimated to approximate $17 billion.[3]

Among the most widely cited yet poorly documented triggers of headache are weather-related variables, such as temperature, humidity, and barometric pressure. Although numerous reports link headache with weather conditions,[4,5] large, well-controlled studies have been mixed in this regard. One large study in Montreal found an association solely with barometric pressure,[6] but this was not confirmed in a case-crossover study in Ottawa.[7]

There is increasing evidence that air pollution, and particularly small particulate pollutants, can induce transient increases in the risk—or triggering—of myocardial infarction,[8] stroke,[9] congestive heart failure,[10] ventricular arrhythmias,[11] asthma,[12] and respiratory infections.[13] A few small studies have suggested that various forms of air pollution may be linked to headache,[14-17]

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as have two Canadian studies that compared trends in hospital visits for headaches and pollutant levels.[6,18] To our knowledge, no studies have evaluated whether ambient air pollution—and particularly fine particulate matter—triggers migraines or other headache syndromes using case-crossover methodology,[19] which directly compares levels of pollutants and meteorologic variables at the time of presentation for headaches to corresponding levels on preceding and subsequent weeks.

To evaluate whether weather conditions and ambient air pollution transiently increase the risk of severe headaches, we conducted a case-crossover analysis of approximately 7,000 patients presenting for emergency care with headache, using levels of ambient air pollution measured continuously at a local site monitor.

METHODS

This study was conducted at Beth Israel Deaconess Medical Center (BIDMC), an academic hospital providing primary and tertiary care in Boston, Massachusetts. The hospital uses an entirely electronic medical record in both the inpatient and outpatient settings. The BIDMC emergency department accounts for approximately 52,000 visits annually.

The BIDMC Committee on Clinical Investigations approved the protocol with a waiver of informed consent. No participants were contacted as part of these analyses.

Study participants. Using administrative data, we identified all 8,235 individuals seen and discharged from the BIDMC emergency department between May 26, 2000 (when an administrative dashboard was instituted), and December 31, 2007, with a primary discharge diagnosis of headache (ICD-9 code 784.0), migraine (codes 346.xx), or tension headache (code 307.81). To minimize exposure misclassification, we excluded individuals who lived greater than 40 km from the hospital (based upon zip code of residence), leaving 7,054 participants eligible for analysis.

Exposure assessment. Exposure to particulate air pollution was based on measurements made at our Boston stationary ambient monitoring site, located on the roof of the Countway Library of Medicine, located less than a half-mile from BIDMC. Daily air pollution concentrations have been measured at this site since 1999 and used in a number of studies.[20-23]

Fine particulate matter with aerodynamic diameter ≤ 2.5 μm ($PM_{2.5}$) was measured continuously using a TEOM (Model 1400A, Rupprecht & Patashnick; Albany, NY). $PM_{2.5}$ measured at this central site monitor have been shown to be strong proxies for personal exposure to particles of ambient origin in communities surrounding Boston.[24,25] Black carbon (BC) was measured continuously using an aethalometer (AE-14, Magee Scientific Inc., Berkeley, CA). Where missing data occurred (~10% of hourly measurements), levels were imputed based on values of adjoining hours and concurrent measurements of correlated pollutants and atmospheric conditions. Hourly nitrogen dioxide (NO_2) and sulfur dioxide (SO_2) were obtained from local monitoring sites operated by the Massachusetts Department of Environmental Protection. Meteorologic data (temperature, relative humidity, and barometric pressure) were obtained from the hourly surface observations of the National Weather Service First Order Station at Logan Airport (East Boston).

Statistical analyses. We used case-crossover analyses to compare measures of weather and ambient air pollution on the day of presentation and control days for each patient. The hallmark of case-crossover studies is self-matching, in which each individual provides his or her own control information and hence confounding by factors that are constant within individuals over the sampling period (e.g., personal medical history) is completely controlled.[26]

We selected control periods according to the time-stratified approach proposed by Lumley and Levy[27] to minimize potential biases due to season and long-term time trends. In this approach, exposure during the 24 hours immediately preceding presentation (or the comparable periods 1–2 days beforehand) was compared to exposure on the three or four other occurrences of that day of the week in a single calendar month.

We used conditional logistic regression models, in which the individual patient was the conditioning factor. We present odds ratios (OR) and 95% confidence intervals (CI) associated with an increment of one interquartile range in 24-hour mean levels of exposure; for interpretability, we also present results for temperature in units of 5°C and pressure in units of 5 mm Hg. We used all headaches as the primary outcome of interest, and tested those with and without a specific discharge diagnosis of migraine in secondary analyses. In all cases, we employed distributed lag models, in which we examined the associations of exposure in the 0–24 hour (lag 0 days), 24–48 hour (lag 1 day), and 48–72 hour (lag 2 days) periods preceding hospitalization simultaneously.

We first examined the associations of meteorologic variables with headaches. We modeled mean apparent temperature at lag 0 with linear and quadratic terms and mean apparent temperature at lags 1 and 2, mean barometric pressure at lags 0–2, and relative humidity at lags 0–2 as linear functions of continuous variables. We next examined the effects of ambient air pollutants in single pollutant models, with lags of 0–2, also as continuous variables. In these models, we adjusted for mean temperature and barometric pressure, using the same lag structure. Given the strong association of season with temperature, we also repeated analyses separately for emergency visits between October and March (cooler) and between April and September (warmer).

RESULTS

Among the 7,054 patients, there were 2,250 with a primary discharge diagnosis of migraine and 4,803 with tension or unspecified headache. In the 7 full years of data collection, the number of participants ranged from 815 in 2004 to 1,033 in 2002. A total of 5,292 (75%) were women. The panel was multiethnic, with 48% white, 23% African American, and 10% Latino; 15% did not have ethnicity recorded. The mean age ($\pm$SD) was 42 $\pm$ 16 years.

Table 1 summarizes ambient levels of meteorologic variables, $PM_{2.5}$, BC, and gaseous pollutants during the time period of the study. Table 2 indicates the pairwise Pearson correlation coefficients among these variables. Among meteorologic variables, temperature correlated moderately with relative humidity but weakly with barometric pressure; relative humidity was inversely correlated with pressure. Lev-

Table 1 Summary of 24-hour averages of air pollutants in Boston, Massachusetts, May 26, 2000–December 31, 2007

	Median	25th Percentile	75th Percentile
Temperature (°C)	11.3	3.6	19.2
Barometric pressure (mm Hg)	761.0	757.0	764.9
Relative humidity (%)	68.1	55.7	80.3
$PM_{2.5}$ ($\mu g/m^3$)	8.6	6.1	12.8
Nitrogen dioxide (ppm)	18.1	14.4	22.5
Sulfur dioxide (ppm)	3.6	2.3	5.5
Black carbon ($\mu g/m^3$)	0.64	0.41	0.92

$PM_{2.5}$ = fine particulate matter with aerodynamic diameter ≤2.5 μm.

els of pollutants tended to correlate at least moderately with each other, particularly for the pairs of NO_2 with SO_2 and $PM_{2.5}$ with BC.

Meteorologic variables. In multivariable models (table 3), higher mean ambient temperature in the 24 hours preceding hospital presentation increased the acute risk of headache (OR for a 5°C increment 1.075; 95% CI, 1.021–1.033; $p = 0.006$). There was no evidence of a nonlinear effect ($p_{\text{quadratic}} = 0.53$), nor were there effects of temperature in the preceding lag periods ($p = 0.71$ for lag 1; $p = 0.34$ for lag 2). Higher temperature increased the risk of cases with both a discharge diagnosis of migraine (OR for a 5°C increment 1.111; 95% CI, 1.013–1.218; $p = 0.03$) and other headache (OR 1.059; 95% CI, 0.994–1.128; $p = 0.08$), and for headaches that occurred in colder months (OR 1.089; 95% CI, 1.016–1.167; $p = 0.02$) or warmer months (OR 1.118; 95% CI, 1.021–1.225; $p = 0.02$). Results were also positive when minimum (rather than mean) temperature in the preceding 24 hours (OR 1.068; 95% CI, 1.014–1.125; $p = 0.01$) or maximum temperature (OR 1.039; 95% CI, 1.014–1.081; $p = 0.05$) were considered. After adjusting for temperature on the 24 hours before hospitalization, there was also no effect of change in temperature in the preceding 24 hours, either in colder or warmer months.

Lower barometric pressure increased the acute risk of headache, but only on a lag 2 scale (i.e., in the 48- to 72-hour period before hospitalization), with an adjusted OR of 0.939 per 5 mm Hg (95% CI, 0.902–0.978; $p = 0.002$). In contrast with temperature, barometric pressure only increased the risk of nonmigraine cases (OR 0.923; 95% CI, 0.880–0.969; $p = 0.001$), and tended to be greater in colder months (OR 0.928; 95% CI, 0.884–0.974; $p = 0.002$). Change in pressure between the 24 and 48 hours before hospitalization did not influence risk in warmer or colder months. There was no association of relative humidity with headache at any lag.

Table 2 Pearson correlation coefficients among meteorologic variables and pollutants in Boston, Massachusetts, May 26, 2000–December 31, 2007

	Temperature	Pressure	Humidity	$PM_{2.5}$	BC	NO_2	SO_2
Temperature	1.00	−0.08	0.94	0.27	0.34	−0.23	−0.55
Pressure		1.00	−0.15	0.01	0.05	0.13	0.14
Humidity			1.00	0.23	0.42	0.01	−0.17
$PM_{2.5}$				1.00	0.70	0.53	0.28
BC					1.00	0.58	0.21
NO_2						1.00	0.61
SO_2							1.00

$PM_{2.5}$ = fine particulate matter with aerodynamic diameter ≤2.5 μm; BC = black carbon.

Ambient air pollutants. Table 3 also presents the risks associated with an increment of one interquartile range in mean levels of ambient air pollutants in the 24 hours before presentation, adjusting for temperature and barometric pressure. Pollutant levels did not influence the acute risk of headache at lag 0 days, either overall or with migraine and nonmigraine cases separately. There was also no significant association of any pollutant with headache on the lag 1 or 2 scales, although NO_2 had a borderline effect on nonmigraine cases on the lag 1 scale (OR for an increment of an interquartile range 1.067; 95% CI, 1.001–1.138; $p = 0.05$). The trend toward higher risk with greater ambient concentration of NO_2 on the lag 1 scale was numerically similar in both colder (OR 1.053; 95% CI, 0.984–1.128; $p = 0.14$) and warmer months (OR 1.062, 95% CI, 0.975–1.157; $p = 0.17$); there were no associations of headache with other pollutants in analyses of warmer or colder months.

DISCUSSION In this analysis of over 7,000 patients, we found that higher ambient temperature transiently increased the risk of headache requiring emergency department evaluation, with approximate 7.5% higher risk for each 5°C increment in temperature. There was also some evidence for higher risk with lower barometric pressure in the 48 to 72 hours before hospital presentation for cases not diagnosed as migraine. We did not find clear association of ambient air pollutants with risk.

Migraine and other headache syndromes have long been linked to weather conditions, particularly with changes in barometric pressure.[4,5] In fact, an association with weather conditions has been suggested as a diagnostic symptom specific to migraine relative to other forms of headache.[28] However, this association was not borne out in a large case-crossover study of migraines in Ottawa,[7] and a large study of headaches not coded as migraines in Montreal also found an association solely with barometric

Table 3 Odds ratios (95% confidence intervals) for total, migraine, and nonmigraine headache requiring emergency department evaluation associated with an increment of one interquartile range in mean exposure level during the 24 hours before presentation

	Interquartile range	Total	Migraine	Nonmigraine
Temperature (°C)	15.6	1.255 (1.066–1.477)	1.389 (1.042–1.852)	1.195 (0.980–1.456)
Barometric pressure (mm Hg)	7.9	1.000 (0.946–1.058)	1.075 (0.973–1.188)	0.965 (0.902–1.034)
Relative humidity (%)	24.6	0.972 (0.912–1.036)	1.018 (0.910–1.139)	0.949 (0.878–1.025)
$PM_{2.5}$ ($\mu g/m^3$)	6.7	1.005 (0.967–1.045)	1.021 (0.956–1.090)	0.997 (0.951–1.045)
Black carbon ($\mu g/m^3$)	0.51	0.995 (0.955–1.036)	1.001 (0.934–1.074)	0.992 (0.944–1.042)
Nitrogen dioxide (ppm)	8.1	0.983 (0.936–1.032)	0.973 (0.892–1.061)	0.988 (0.931–1.049)
Sulfur dioxide (ppm)	3.3	0.975 (0.933–1.018)	0.988 (0.916–1.065)	0.968 (0.917–1.022)

$PM_{2.5}$ = fine particulate matter with aerodynamic diameter ≤2.5 μm.

pressure.[6] These results together with ours suggest that the association of headache with barometric pressure is unlikely to be a useful diagnostic marker specific for migraine.

We also found a strong association of headache with ambient temperature, regardless of the discharge diagnosis coded. The one previous large case-crossover study of migraines did not find such an association but examined only a single temperature cutpoint of 19.6°C.[7] However, other studies have found generally higher rates of migraine in warmer seasons,[29-31] despite an association of higher temperature with lower blood pressure.[32,33] Whether higher temperature is also associated with a greater likelihood of triggering the more common headaches that do not result in emergency department evaluation will require additional study.

There is growing interest in air pollution as a trigger of a variety of acute health conditions. Air pollution represents a complex mix of pollutants, including both coarse and fine particles and gaseous constituents. Two common pollutant gases, sulfur and nitrogen dioxides, were positively associated with emergency visits for nonmigraine headache in similar time-series studies in Ottawa and Montreal, with higher risks seen across multiple lag scales.[6,18] Our results tend to support the higher risk associated with NO_2 exposure, where higher risk was seen specifically for headaches not diagnosed as migraine.

We anticipated that $PM_{2.5}$ might have the strongest association with headache, as they appear to induce sympathetic nervous system activation (best studied in relation to heart rate variability[34]), pulmonary and subsequently systemic inflammation,[35,36] and vascular endothelial injury.[37,38] They have also been most closely associated with triggering cardiovascular events.[39] In the one previous large-scale study of headaches, $PM_{2.5}$ only increased risk on a lag 2 scale, with a generally weaker effect than observed for gaseous pollutants.[6] Given the marked effects of fine particulate matter observed in previous studies of cardiovascular disease, the role of these particles as a trigger of headache clearly merits additional study.

It is also important to recognize the expected magnitude of effect when considering the lack of statistical association between pollutants and risk in our study. In general, previous case-crossover studies of fine particulate air pollution and cardiovascular conditions such as ischemic stroke[9] have demonstrated approximately 1% higher risk (i.e., relative risk of 1.01) with an interquartile range increment similar to that used here. The precision of our estimates was generally insufficient to exclude an effect of that magnitude, and hence we cannot rule out an association that, albeit small in magnitude, could have far-reaching public health implications.

The clinical and public health implications of our findings even for temperature may differ to some degree. Our results suggest that an increase in temperature of 5°C would confer a short-term 7.5% increase in risk. This magnitude of excess risk is obviously modest and may not be an important factor in the clinical management of individual patients, given the many other potential triggers of migraine that patients may face. At the same time, every member of a given geographic region is repeatedly exposed to this excess risk, and hence the public health impact of triggering migraine by rising ambient temperatures may be greater than exposures that confer a higher relative risk but to a much smaller number of potentially exposed patients.

This study has several potential limitations, most of which were likely to have potentially biased our results toward the null. First, we relied upon headaches classified by emergency department physicians, and hence misclassification of some admissions—and particularly for comparisons of cases coded as migraine or not[40]—is likely. Second, we relied upon use of a central ambient monitor rather than personal exposure measures, although levels of SO_2 and

$PM_{2.5}$ in particular tend to be spatially homogenous within our region of study. Third, we had highly accurate information on the time of hospital presentation but not about the timing of actual symptom onset, and hence could not account for the variable duration of time that patients experienced headaches before evaluation. Finally, because this study relied upon patients seen for headaches requiring emergency evaluation, we cannot distinguish whether observed increases in risk related to temperature or barometric pressure reflect changes in the incidence of headaches or in their severity.

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